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MEDICAL

The American Journal of

DIGESTIVE DISEASES

March 1956

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Klotz: Depression of Gastric Secretion by a New Anticholineraic Agen

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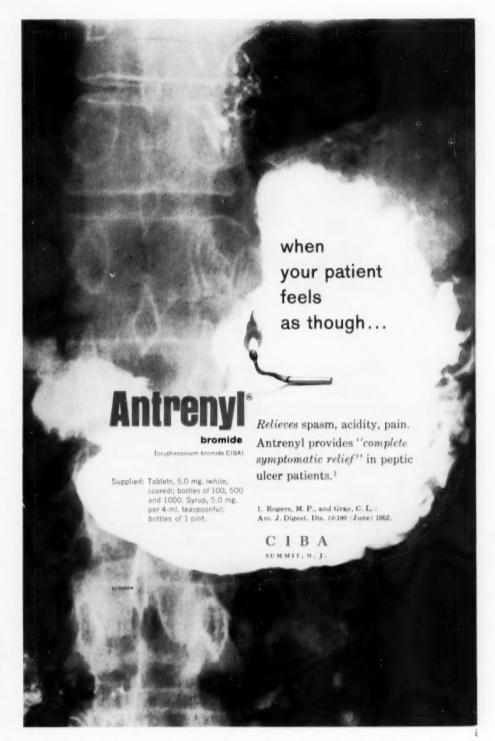
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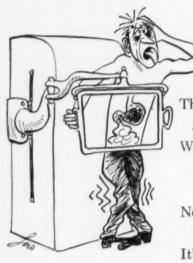
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The American Journal of

DIGESTIVE DISEASES

The American Journal of Digestive Diseases is a clinical journal edited primarily for physicians and surgeons engaged in active practice and concerned directly with diagnosis and care of patients. It is devoted to prompt publication and dissemination of soundly based investigation and clinical study in the field of Gastroenterology broadly defined. The Journal includes within its scope the practical aspects of diseases of the digestive system, including nutritional and metabolic disturbances and diseases of the liver.

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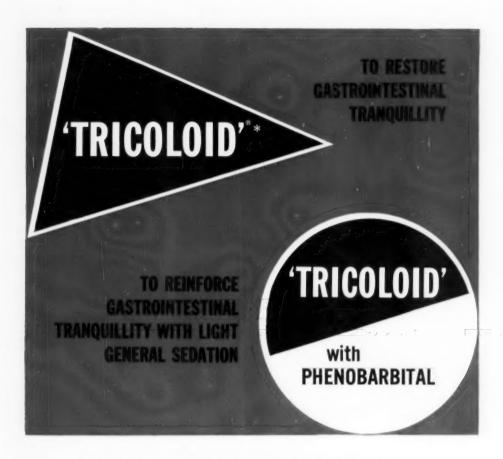
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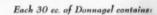
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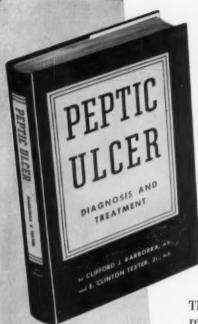
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Pneumatosis Coli

RICHARD H. MARSHAK, M.D., AND JOAN ELIASOPH, M.D.

PNEUMATOSIS COLI is a rare disease manifested by intramural collections of gas in the colon and its peritoneal attachments. Pneumatosis intestinalis is the more general term applied to the same condition involving any portion of the intestinal tract. Clinically and pathologically, the cases have been divided into primary and secondary forms. The primary form occurs without apparent cause and usually shows diffiuse involvement of the bowel wall and mesentery. The secondary form is more common and is frequently related to some other identifiable lesion of the gastrointestinal tract such as peptic ulcer or carcinoma of the stomach.

In 1952 the world literature was reviewed by Koss, who found a total of 213 reported cases of pneumatosis intestinalis. Of these, 125 patients had involvement of the small intestine, 9 had involvement of both the small and large intestine, in 34 the ileocecal region was involved, and in 13 the large intestine and its peritoneal attachments were affected. The localization of the disease in the colon was not further defined. Since that time, a few cases reporting involvement of the left side of the colon have appeared in the literature.^{1, 2, 5, 6, 7, 3} Because the colon is involved so infrequently in this disease, we are presenting 4 new cases of pneumatosis coli involving only the left side, with comments on the clinical and roentgen findings. On the basis of these cases possible mechanism of causation of this condition are suggested.

Pathology

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The gas pockets are found in the intestinal wall and are most often visible over the serosal surface of the bowel, occurring singly or in clusters and varying greatly in size. They may be sessile or pedunculated, round or sausage-shaped. Less often they are found in the submucosa, and then generally in association with serosal involvement. The muscularis is rarely involved.

Microscopically, the mucosa of the involved bowel segment is intact. The cysts are considered to be dilated lymph channels filled with

From the Department of Radiology, The Mount Sinai Hospital, New York, N. Y.

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Marshak & Eliasoph

gas and are lined by endothelial cells with an occasional large, multinucleated giant cell. Varying degrees of inflammatory response may be present, ranging from a minimal round-cell response to active inflammation and granuloma formation with epithelioid cells.

Associated Lesions

In most of the cases with involvement of the small intestine and ileocecal region there is an associated lesion of the gastrointestinal tract, usually a stenotic lesion in the pyloric region of the stomach. Other associated diseases which have been observed are appendicitis, tuberculous enteritis, gastric ulcer, and gastric carcinoma. In the few cases reported of pneumatosis involving the left colon, no upper gastrointestinal lesion has been found.

Complications

Complications such as pneumoperitoneum due to perforation of the gas cysts, intestinal obstruction due to compression of the bowel lumen by the cysts, or volvulus have been observed when the disease affects the small intestine and ileocecal region. This has not been noted with left-sided pneumatosis coli.

ROENTGEN FINDINGS

Pneumatosis coli usually is asymptomatic and discovered incidentally during a course of study for unrelated conditions. The roent-gen criteria for its diagnosis are well defined, and it should not be confused with other conditions including carcinoma. The roentgen findings in pneumatosis involving the small intestine have been discussed in the literature; however, few cases of pneumatosis involving the left colon have been described. Because the course of pneumatosis coli when it involves the left colon is chronic and benign, it is important to recognize the roentgen picture as this may be the sole means of diagnosing the condition without resorting to surgery.

A preliminary film of the abdomen may reveal an unusual cluster of gas shadows which may be grapelike in pattern or may simulate a normal intestinal pattern. The alterations may be obscured by normal intestinal shadows. Barium studies of the colon will demonstrate that the gas shadows lie adjacent to the intestinal lumen and indent its contours. The defects are variable in size and may extend into the mesentery. The mucosal pattern may be distorted by the intramural masses but the folds are intact. The bowel segments involved by pneumatosis may not be continuous, and in one case reported here the sigmoid and splenic flexures were involved, and the intervening bowel

Pneumatosis Coli

segment was normal. The roentgen findings are constant and do not vary from one examination to another, nor have they shown a tendency to change over a course of years. Follow-up studies, up to 4 years, have shown no change from the initial study. In none of our patients have complications such as pneumoperitoneum or intestinal obstruction been observed.

ETIOLOGY

Many theories as to the etiology of pneumatosis intestinalis have been considered. The neoplastic theory, which suggests that the intramural gas is produced by "gas-forming" neoplastic cells, has been discarded. The theory that "gas-forming" bacterial organisms invading the bowel wall produce intestinal emphysema has not found satisfactory bacteriologic and pathologic confirmation. Masson suggested that local alterations in the acid-base balance in the intestinal lumen might account for the release of gases into the intramural lymphatics. The theory of dietary deficiency as a cause of intestinal emphysema is based on the observation that in hogs fed a diet of polished rice it is possible to produce intestinal gas cysts identical to those seen in pneumatosis intestinalis. In most human cases, there is often an associated lesion in the upper gastrointestinal tract, most often a stenotic lesion in the antrum, with resultant inadequate nutritional intake.

Mechanical Theory

The mechanical theory applies in those cases of pneumatosis intestinalis which have an associated gastrointestinal lesion with a mucosal defect and possibly obstruction. In the case of obstructing gastric or duodenal ulcers, it has been suggested that gas under higher intraluminal pressure is forced through the mucosal defect into the submucosa and serosa and dissects along the mesenteric lymphatics to a site distant from the original lesion. These are the secondary forms of pneumatosis intestinalis. In the primary form, which most often involves the ileocecal region, there is no known concomitant lesion. It has been speculated, however, that if this region were examined pathologically the appendix might disclose a portal of entry.

Traumatic Theory

In pneumatosis involving the left side of the colon, there has been little consideration of the possible causes. Five cases recently reported in the literature were reviewed in an attempt to determine the possible role of mechanical trauma to the colonic mucosa in the production of

Marshak & Eliasoph

pneumatosis. In 2 of these cases, there had been a sigmoidoscopy prior to the onset of the pneumatosis, and in 1 of these a mucosal biopsy was performed.^{3, 7} In the latter case, barium enema the day of biopsy revealed no evidence of pneumatosis coli. One week later, however, the lesion was present. The diagnosis was confirmed at operation. In the third case the disease may have antedated sigmoidoscopy⁶ and in the fourth, sigmoidoscopy was not performed.⁸ In the fifth patient, an acute onset followed rectal surgery.¹

Three of the 4 patients in this report had pneumatosis involving the sigmoid and all 3 had been sigmoidoscoped. Two were biopsied. The fourth patient had pneumatosis localized only to the splenic flexure of the colon and had no history of sigmoidoscopy or other local trauma.

The relationship between sigmoidoscopy and the anatomic site of the pneumatosis is so striking as to suggest an etiologic factor in the sigmoidoscopy. Since a mucosal defect is most often found in association with pneumatosis elsewhere in the gastrointestinal tract, it appears likely that the trauma of sigmoidoscopy with and without biopsy may be responsible for the production of pneumatosis of the left side of the colon. The predisposing factor to this condition which accounts for its extreme rarity remains elusive.

CASE REPORTS

Case I

A 55-year-old woman was admitted to the hospital with the chief complaint of rectal bleeding of 3 weeks' duration. Aside from an appendectomy 25 years earlier, the past history was unremarkable. Physical examination revealed only a well-nourished patient with internal hemorrhoids. Sigmoidoscopy revealed a granular mucosa in the rectosigmoid area, and a specimen was taken for biopsy. The examination was otherwise negative. When the sigmoidoscope was withdrawn this patient developed severe, generalized abdominal pain. Palpation of the abdomen revealed diffuse tenderness, maximal over the left side. The sigmoid could be felt as a doughy mass in the left lower quadrant.

Roentgen study shortly thereafter, including barium enema, revealed the typical findings of pneumatosis coli involving the sigmoid without other significant abnormality. There was no evidence of free intraperitoneal gas (Fig. 1). The symptoms of abdominal pain subsided gradually and disappeared in about a week without specific therapy. Follow-up roentgen studies (Fig. 2) over a 4-year period have shown no change in the degree of extent of the pneumatosis coli demonstrated at the initial study.

Pneumatosis Coli

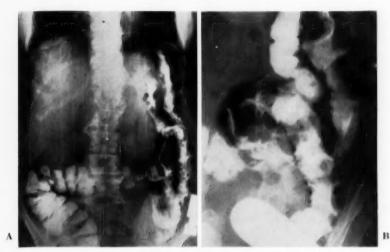


Fig. 1. Case 1. 4, the initial barium enema demonstrating air cysts in the wall of the descending colon and sigmoid. B, close-up showing indentation of the bowel contours by the intramural gas collections.

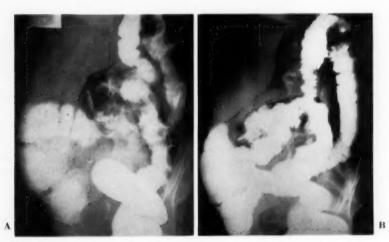
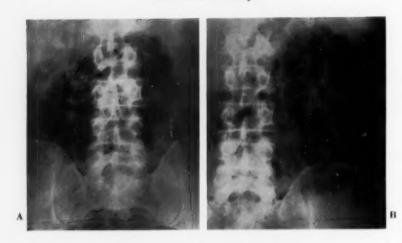


Fig. 2. Case 1. A, follow-up examination 3 years later demonstrating no change in the interim since the first study. B, follow-up examination 4 years later showing again no change from the previous studies.

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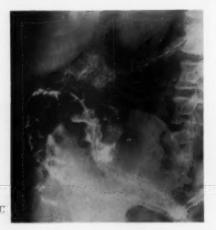


Fig. 3. Case 2. A, flat film of the abdomen reveals a cluster of gas shadows occupying the midabdomen. B, subsequently the gas shadows are found in the left upper quadrant. C, barium enema studies demonstrate the gas within the wall of the redundant sigmoid.

Case 2*

A 58-year-old white male entered the hospital for a work-up because of several days of painless urinary bleeding. The only positive finding in the

^{*} The authors are grateful to Drs. Harry A. Solomon and S. Daniel Blum for permission to present this case,

Pneumatosis Coli

past history was a hemorrhoidectomy 4 years before. He had never had abdominal x-rays. The physical examination was essentially negative and the presence of red blood cells in the urine was the only pertinent laboratory finding. During the course of work-up, he was proctoscoped to 7 inches. Findings were normal. There were no biopsies.

Four days following this procedure intravenous urography was performed. Grapelike clusters of gas were noted in the mid abdomen (Fig. 3A). The upper urinary tracts were normal but there was a filling defect in the bladder shadow that was subsequently identified as a benign papilloma. Subsequent x-rays showed migration of the gas pockets into the left upper and then into the right lower quadrants (Fig. 3B). Upper gastro-intestinal barium studies were normal but barium enema disclosed abnormalities pathognomonic of pneumatosis coli in a very mobile sigmoid. A second, smaller and less advanced area of involvement was noted in the splenic flexure (Fig. 3C). No other lesions were demonstrated. Three-month follow-up studies were identical.

Case 3

A 52-year-old male entered the surgical service because of bright-red rectal bleeding of brief duration. He had an appendectomy several years before. Barium enema had been carried out some time prior to admission



Fig. 4. Case 3. Barium enema (post-evacuation film) demonstrates the marked alterations in mucosal pattern and contour of the sigmoid involved by pneumatosis.

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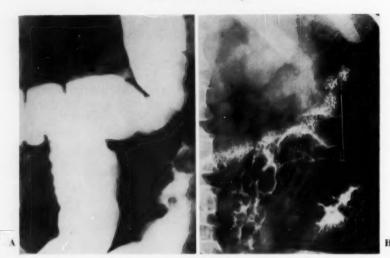


Fig. 5. Case 3. A, the barium-filled sigmoid shows the contour changes caused by the gas cysts. B, the mesentery of the sigmoid also contains numerous gas cysts.

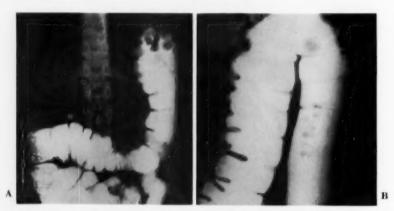


Fig. 6. Case 4. A, localized involvement of the splenic flexure by pneumatosis. B, close-up of splenic flexure showing characteristic roentgen findings in the barium-filled bowel.

and was negative. At the time of entry, physical examination and laboratory data were noncontributory. At sigmoidoscopy a solitary polyp was encountered 6 inches from the anus and was resected. Barium enema was repeated subsequently and revealed pneumatosis involving the sigmoid

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and its mesentery (Figs. 4 and 5). Follow-up roentgen studies 6 months later and 2 and 2½ years later have shown no change and the patient has remained asymptomatic.

Case 4

A 56-year-old woman entered the hospital for investigation of alternating diarrhea and constipation of 9 weeks' duration. The past history and physical and laboratory findings were not noteworthy. There was no history of rectal surgery. Barium study of the colon showed changes in the distal transverse colon and splenic flexure characteristic of pneumatosis coli (Fig. 6). No other clinical or roentgen findings could be identified to account for the patient's admitting complaint. Her condition has remained clinically unchanged over a 3-year period of observation, as have the roentgen findings.

SUMMARY AND CONCLUSIONS

The incidence, pathology, and roentgenology of pneumatosis involving the left side of the colon have been discussed.

The possible causes of pneumatosis intestinalis have been reviewed. There has been little consideration in the literature of the etiologic factors in left-sided pneumatosis coli, and it is suggested that local trauma to the rectal or sigmoid mucosa may be important. In support of this, several cases from the literature are cited and 4 additional cases presented.

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Depression of Gastric Secretion by A New Anticholinergic Agent

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Many anticholinergic gastric secretory depressant medications are now available. Among other considerations the importance of hydrochloric acid in the genesis of peptic ulcer has made this expanding group of pharmaceutical compounds of considerable current interest. To choose one for therapy is often difficult because precise knowledge of its total pharmacologic action is frequently unavailable. Clinical use is based mainly upon antispasmodic or antisecretory potency. A subjective symptomatic evaluation of these drugs may be grossly misleading. The present paper is a study of one aspect of the pharmacology of a 3-hydroxy-piperidine derivative, N-ethyl-3-piperidyl-benzilate methobromide, measuring its effect on gastric secretion in man.

PHARMACOLOGY

N-ethyl-3-piperidyl-benzilate methobromide is a synthetic anticholinergic agent.* It is a quaternized derivative of 3-hydroxy-piperidine and is a postganglionic depressant similar to atropine. It is rapidly absorbed from the gastrointestinal tract of animals with duration of effect extending over 2 to 3 hours. Absorption studies have shown that acetylcholine-induced vasodepression is partially inhibited within 5 minutes and completely blocked in 10 to 15 minutes after 0.5 mg./ Kg. body weight is injected into the lumen of the stomach and of the small bowel of dogs. These results are similar to atropine except that they last about 30 per cent longer.

It is described as being equivalent to atropine in protecting the guinea pig against bronchospasm and in relaxing spontaneous as well as prostigmine-induced intestinal contractions in the dog. Intravenous

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The author is indebted to Miss Melva R. Duvall for her valuable technical assistance. *Available as Piptal (Lakeside).

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injections in dogs up to 1 mg./Kg. produce no adverse effects. This amount is many times that required for full action of the drug.

MATERIAL AND METHOD

"Acute" Studies

Patients with duodenal ulcer and others with known high gastric secretion were chosen from the hospital ward for this study after an initial gastric analysis had demonstrated the gastric secretory pattern in each. Such patients served as critical assays for the effectiveness of the drug on gastric secretion. These tests were designated as "acute" studies. As the investigation progressed some low secretors were tested also to see what effect the drug might have on a low-secretion pattern.

All patients were fasted from midnight. A Levin tube was passed in the early morning and the fasting residual was removed and saved. Thereafter 4 15-minute fractions of gastric juice samples were collected by constant hand suction. This series of 5 specimens constituted the basal gastric analysis.

The test medication was then instilled intragastrically by the Levin tube and 1 hour was allowed to elapse for drug absorption before further samples were removed. Hand suction was again resumed for the collection of 15-minute fractions for the following 2 hours.

Volume, free acid in clinical units, total acid, and milliequivalents of acid were then measured in each sample. Milliequivalents of acid in the 4 basal hour fractions were then compared with milliequivalents of acid in the hour collection following instillation of the medication.

Dosage

Various dosages of the anticholinergic drug were used. When it became apparent that 5 mg. caused no noticeable side effects, the dosage was increased to 15 mg. and finally to 20 mg. in the acute studies. Eighty-eight patients were studied in this manner.

"Chronie" Studies

A second series of 20 patients was followed over a number of months with serial gastric analyses in a "chronic" study. All of these were patients with duodenal or pyloric canal ulcers under intensive medical management. These patients were given 5 mg. dosages of the drug 4 times daily. Basal 1-hour gastric analyses were obtained at 2- to three-week intervals and, in many, a second hour gastric analysis

was obtained after stimulation with a histamine analog, 3-beta-amino-ethylpyrazole dihydrochloride.

Comparative Study

A small comparative study was then performed on a few patients with 2.5-mg. and 5-mg. dosages of methscopolamine bromide, another known potent anticholinergic medication. This medication was chosen since its potency is well documented.

RESULTS

Decrease in Acid Output

"Acute" Studies

In 77 of the patients in the "acute" studies, the gastric acid output was decreased after instillation of the medication as compared to the basal hour. Sixty of the patients had a decrease in acid output to one half or less than one half of the basal. Thirty-five patients had anacidity for 30 minutes or longer (Table 1).

In a few cases there seemed to be a delayed effect of the medication on the gastric secretion with a depression appearing in the third hour collection. This was also considered as showing a decrease in gastric acid output since the trend seemed unequivocal. This "delayed reaction" may reflect some difference in absorption of the medication. Decreasing volumes of gastric juice generally paralleled the decrease in free acidity.

Several patients had repeat analyses with increasing dosages of the drug. A larger dose sometimes had less effect than a small dose, demonstrating a variability of response to the medication in the same patient and showing that larger dosages do not necessarily increase the inci-

TABLE 1. Effect of N-ethyl-3-piperidyl-benzilate Methobromide on Basal Gastric Secretion

Dose (total mg.)	5	15	20	Total
No. of patients	12	15	61	88
No. of patients showing anacid- ity (40%)	8 (66%)	4 (27%)	23 (38%)	35
Duration of anacidity (min.)				
30-60	5	3	6	
60-120	2	1	3	
120-180	1	0	14	
Decrease in mEq. of free acid (20%)	1	3	13	17 (88%)
Decrease in mEq. of free acid to 12 or more (68%)	10	8	42	60)

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dence of anacidity. However, larger doses of anticholinergic drugs have been reported to prolong duration of anacidity when it occurs.² It was quite evident that very small doses could produce maximum effects of prolonged anacidity in susceptible individuals.

"Chronic" Studies

The 20 "chronic" studies were undertaken to see what changes in secretion might occur in individuals taking frequent dosages over a

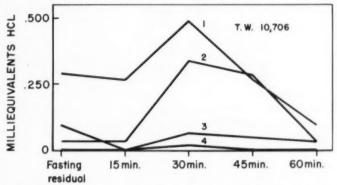


Fig. 1. Basal gastric secretion in patient taking 5 mg. of N-ethyl-piperidyl-benzilate methobromide for 3 months. Decreased secretion of acid.

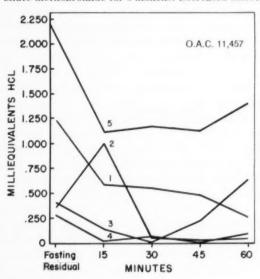


Fig. 2. Basal gastric secretion in patient taking 5 mg. of N-ethyl-piperidyl-benzilate methobromide for 3 months. Decreased secretion of acid followed by rise.

TABLE 2. Effect of Methscopolamine Bromide on Basal Gastric Secretion

Dose (total mg.)		2.5		5	T	otal
No. of patients	10		5			15
No. of patients showing anacidity (47%) Duration of anacidity (min.)	3	(33%)	4	(80%)		7
30-60	1		1			
60-120	1		0			
120-180	1		3			
Decrease in mEq. of free acid	0		0		0,	87%
Decrease in mEq. of free acid to 1/2 or more	9		4		13)	

long period of time. Only a few showed a comparative decrease from the original basal gastric analysis during the observation period of several months. Results in a representative patient are shown in Fig. 1. Where a comparative decrease occurred, higher values were usually noted at the end of three months (Fig. 2), but often as early as the first month. No depression of histamine-analog stimulation appeared at any time.

Comparative Study

The small comparative series of 15 patients was given methscopolamine bromide as in the acute studies. The usual 2.5-mg. dose was given to 10 patients and 5 mg. given to 5 patients (Table 2). Comparison of these results with those obtained with N-ethyl-3-piperidyl-benzilate methobromide (Table 1) shows that the range of effectiveness of the two agents is quite similar.

Side Effects

Side effects of anticholinergic drugs may constitute a major patient objection. Dryness of the mouth and blurring of vision are frequent complaints. In the older male patient, acute urinary retention is not uncommon. Paralytic ileus has been observed. Statements are made in the literature that undesirable side effects almost invariably accompany the more effective gastric secretory depressant drugs and imply that these disadvantages are to be accepted as inevitable accompaniments.

No side effects were elicited in any of the patients in the present studies and, as has been mentioned, many of the "acute" studies employed four times the usual dosage. Patients taking the medication for the "chronic" studies were totally free of any side effects.

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DISCUSSION

The therapeutic efficacy and desirability of currently used anticholinergic drugs are limited by certain unpredictable variations. One measurement of pharmacologic potency, the effect of the medication on basal gastric secretion, has been used in this particular study. Variable results were found to occur in the same patient from day to day with the same dosage of drug. At times a smaller dose had a greater effect than a larger dose. Furthermore, in considering depression of gastric secretion by anticholinergic agents, basal secretion is a relatively unstimulated type of secretion; it is probably more amenable to suppression by the medication and certainly is not representative of the behavior of the stomach throughout the day. Measurement of effect on basal secretion provides no clue to possible suppression of food-stimulated secretory flow.

Duration of Effect

N-ethyl-3-piperidyl-benzilate methobromide is interesting from several points of view. These studies demonstrate its effect on volume of gastric juice and milliequivalents of free hydrochloric acid.

The "chronic" cases in this study suggest that there is no enduring or cumulative effect of the agent in suppressing the total output of free hydrochloric acid in the customarily prescribed dosages. They demonstrate the inadequady of these dosages to control gastric acidity consistently. It was apparent in these "chronic" patients that the use of the anticholinergic agent did not inhibit the histamine-analog since an increase in volume and free acidity was eventually observed in almost all of the patients. Occasionally a lower volume was obtained; however, the free acid output was unaltered.

Anacidity and Decreased Free Acidity

In the small comparative series of patients where methscopolamine bromide was employed, the frequency of anacidity was similar to that of N-ethyl-piperidyl-benzilate methobromide in the 5-mg. dosage. Although only a few patients were tested, the similarity in potency of the two medications is apparent. These results are in essential agreement with previous reports on methscopolamine (Pamine) bromide.³

The most desirable results in this study were those demonstrating a complete suppression of free acid after the instillation of the medication (Table 3). A more usual result, however, was a decrease in the free acidity without the appearance of anacidity.

TABLE 3. Anacidity Following Intragastric Instillation of N-ethyl-piperidinebenzilate Methobromide

2	Specimen	Volume (cc.)	Free acid (c.u.)	Total acid
Basal		A C		
fastir	g residual	16	26	34
1.0	15 min.)	16	13	26
2	6.6	29	45	58
3	6.6	46	2	17
4	44	3	9	21
Hour	arter A ethyl-pip	eridine-benzilate metho	obtoinide (20 mg.)	
			0	9
1 (15 min.)	51		9
1 ()	15 min.)	51 16		9 6 11
1 () 2 3	15 min.)	51		9 6 11 2
1 (1 2 3 4	15 min.)	51 16		9 6 11 2 2
1 (1 2 3 4 5	15 min.)	51 16		6 11 2
1 (1 2 3 4	15 min.)	51 16		6 11 2 2
1 (1 2 3 4 5 6	15 min.)	51 16		6 11 2 2 2 2

Role of Anticholinergies in Peptic-Ulcer Management

Although anacidity is probably highly desirable when anticholiner-gic agents are used in peptic ulcer management, a decrease in 24-hour acid output, although not anacidity, may be important in the management of ulcer. Patients with duodenal ulcer ordinarily have elevated gastric secretory patterns, and conventional treatment employs antacids throughout the day to control this free acid. It is generally delieved that sufficient antacid medication during the day will permit the ulcer to heal even though no antacid is used regularly during the night. Frequent doses of potent anticholinergic agents could theoretically reduce the 24-hour output of free acid to within the range of a reduced free acidity produced by frequent doses of antacids. This hypothesis, however, would have to be tested with anticholinergic medications by 24-hour gastric-secretion studies.

Management of the patient with peptic ulcer requires long-term supervision. Consequently, avoidance of parenteral medication is highly desirable and an oral medication is an important requisite in any satisfactory agent for suppression of gastric secretion. No parenteral medications were used in the present study.

The over-all observations emphasize the concept that anticholinergic agents are adjuncts to, not substitutes for, adequate antacid management in the treatment of peptic ulcer.

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SUMMARY and CONCLUSIONS

The anticholinergic medication N-ethyl-3-piperidyl-benzilate methobromide (Piptal) was studied in 88 patients with elevated and normal gastric secretory patterns. In 77 (88 per cent) of the patients there was a decrease in the output of free acid as compared to the basal hour. In 35 patients (40 per cent) anacidity for 30 minutes or longer was produced.

In no cases were there complaints of any side effects in this study. Piptal is apparently unique in that it represents a potent antisecretory agent without side reactions.

Patients show varied responses to the same dosage of the drug, and larger dosages do not necessarily increase the number of patients on whom the drug will have an inhibitory effect. Probable anticholinergic escape appeared in some patients after an unknown period of time. Prolonged use did not consistently or permanently depress basal gastric secretion.

Presently available anticholinergic drugs serve as an adjunct in the treatment of peptic ulcer, not as a substitute for effective antacid management. Further pharmacologic development may be expected to produce highly potent antisecretory agents without undesirable side effects. Piptal is a desirable development in this general direction.

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Abnormal Swallowing in Central-Nervous-System and Neuromuscular Disease

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The normal swallowing mechanism has occupied a good deal of attention over a period of years. Papers and monographs by Barclay,^{2, 3} Magendie, Cannon, Negus, and Templeton have contributed in a noteworthy manner to our knowledge about this area. Recently Ramsey *et al.* have aroused interest in the use of cinefluorography in examination of the pharyngoesophageal region.

For the past several years we have been interested in the problem of abnormalities of the swallowing mechanism found in disorders of the central nervous system and neuromuscular diseases. These have been demonstrated by roentgen examinations of the oropharyngoesophageal area after oral ingestion of barium. Detailed description of the anatomy of this area is readily available in the standard texts and needs no further description.

THE SWALLOWING MECHANISM

The physiology of the swallowing mechanism is complex and not always too clearly understood, but certain salient features may be emphasized for purposes of this presentation, particularly relating to the oropharyngoesophageal region.⁵

Although the mechanism of deglutition is divided into three phases, we are concerned here only with the first two phases whereby the bolus is passed from the mouth into the thoracic esophagus. In the first or buccopharyngeal phase (under voluntary control), the bolus is thrust from the mouth into the pharynx by the action of the tongue assisted by contraction of the mylohyoid muscle.

The second phase is short, with continuing inhibition of respiration

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initiated during the first phase. The bolus is passed through the pharynx into the esophagus with the aid of reflex muscular movements which prevent its entrance into the mouth, nasopharynx, or larynx and cause relaxation of the cricopharyngeal muscle. The bolus travels at a speed of approximately 33 cm. per second into the cervical esophagus where it is found 0.5 to 1.0 second after initiation of the swallowing act. The bolus reaches the thoracic esophagus in about 2 seconds after leaving the mouth and requires about 7 seconds to pass from the mouth into the stomach. Although gravity is of importance in the esophageal phase, Schreiber in 1915 showed that it played no significant role in the buccopharyngeal phase.

The swallowing reflex originates in the mucosa in the area surrounding the entrance into the pharynx. The afferent fibers of this central nerve reflex are supplied by branches of the trigeminal, glossopharyngeal, and the pharyngeal and superior laryngeal branches of the vagus. This central reflex cannot be initiated by a bolus placed directly in the esophagus.

The central nervous system deglutition center has been localized in the region of the floor of the fourth ventricle. Thus, if the center or the central nerves associated with it are damaged or destroyed by any of a variety of lesions of the central nervous system deglutition will no longer be normal.

NEUROPATHIC ASSOCIATIONS

Pharyngoesophageal symptoms may be the first indication of neurologic disease. Otell and Coe in 1935 showed roentgenologically that in various cranial nerve diseases, bulbar lesions, poliomyelitis, and myasthenia gravis only the proximal one third of the esophagus and the pharynx was involved, whereas the middle third and distal third were normal. In such cases these investigators were able to detect and describe a number of the changes occurring in the swallowing mechanism which we will illustrate below. Their contribution was rather remarkable inasmuch as the observations were based on the available conventional technics—fluoroscopy and standard roentgenography.

Schwab and Viets in 1947 and Baker and Christoferson in 1950 emphasized the relationship of dysphagia to myasthenia gravis and to cerebellopontine angle tumors. As far as we can determine, there are no definitive roentgen studies of the oropharyngoesophageal region in neurologic and neuromuscular diseases except for the work of Otell and Coe.

Poppel et al.

Our presentation, then, mirrors an attempt to delineate graphically the changes in the oropharyngoesophageal area in some of these diseases, using normal standards as a base line for comparison. This report is of a preliminary nature and represents the initial phase in a continuing investigation.

TECHNIC

We decided on the use of the Fairchild camera apparatus to delineate adequately the oropharyngoesophageal area after oral ingestion of barium. The technic consists in placing the patient in a sitting position in front of the Fairchild camera. A mouthful of semithick barium paste (of the consistency of cream) is given to the patient who is then instructed to swallow.

Centering over the pharynx and upper esophagus, we are able to take 2 exposures per second. We have determined that 1 exposure per second, or in most instances 1 exposure every 2 seconds up through 20 seconds, constitutes an adequate examination. Initially we used both frontal-plane and lateral projections, but we now find the lateral view preferable.

CASE MATERIAL

Forty normal adults were examined to establish the roentgen appearance in the oropharyngoesophageal area after a barium swallow.

Forty-one patients with varying degrees of neurologic and neuromuscular disorders (Table 1) were roentgenologically examined with reference to the same area. No attempt was made to relate the severity of the illness to the findings, but necessarily we dealt with ambulatory and relatively cooperative patients.

TABLE 1. Neurologic and Neuromuscular Disorders in 41 Patients Examined Roentgenologically

Paralysis agitans	8
Multiple sclerosis	7
Muscular dystrophy	7
Amyotrophic lateral sclerosis	6
Myasthenia gravis	5
Hemiplegia	3
Dystonia muscularis deformans	1
Posterolateral sclerosis	1
Myotonia dystrophica	1
Epileptiform degeneration	1
Numbness of undetermined origin	1

Abnormal Swallowing

FINDINGS

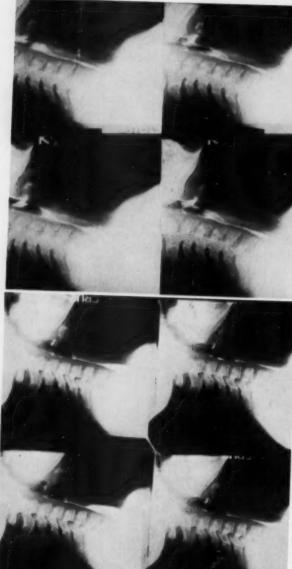
Normal

In the normal patient the swallowing act is initiated without difficulty and the bolus is swallowed easily with a single movement (Figs. 1 and 2). Barium reaches the pharyngoesophageal region within a fraction of a second to 2 seconds after initiation of swallowing. The opaque material coats the entire pharynx uniformly after the initial swallowing act, with no significant stasis or retention in the pharynx, pyriform sinuses, or vallecula and with no abnormal widening or ballooning of these structures. A thin coating through the pharynx may be noted as much as six seconds after swallowing. The barium is distributed uniformly with no evidence of increased mucus content.

Abnormal

In the 41 patients with diseases of the central nervous system or neuromuscular diseases, a number of nonspecific abnormalities of the swallowing mechanism with abnormal changes in the oropharyngoesophageal region was demonstrated (Figs. 3–8). Following is a summary of these deviations:

- Difficulty in initiating the swallowing act due to some loss in the over-all coordination of this complex mechanism.
- 2. Inability to swallow the bolus uniformly, resulting in abnormal segmentation and loss of the normal smoothly flowing bolus.
- 3. Inability to swallow except in the upright posture.
- 4. Regurgitation.
- Churning effect. In this phenomenon, small amounts of barium may rapidly move up and down a number of times in the pharynx and upper esophagus.
- Patchy and irregular coating of the pharyngeal walls due to increased salivary secretion. The increased mucus content interposes between the barium and the mucosa.
- Spasm, producing irregular narrowed segmentation. This finding is most common at the junction of the pharynx and esophagus at the level of C₆.
- 8. Disturbances in transit time. A delay in propulsion of the bolus results in abnormal stasis and consequent retention in the oropharynx, epiglottic vallecula, and pyriform sinuses and unusual delay in the inferior pharyngeal segment. In some instances the inferior pharyngeal segment continues to widen until the increased hydrostatic pressure opens the narrowed pharyngoesophageal



Figs. I and 2. Demonstration of deglutition in normals with bolus passing rapidly into thoracic esophagus. Sequence of films in Fig. 1 taken at 2, 4, 6, and 8 sec., in Fig. 2 at 2, 5, 6, and 7 sec.

Abnormal Swallowing

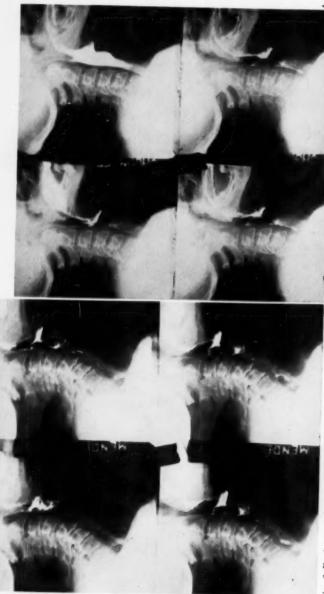
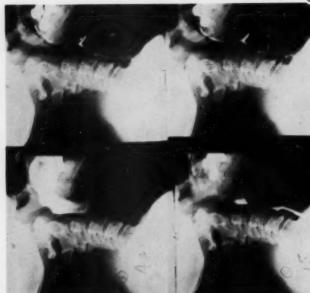


Fig. 3. Patient with amyotrophic lateral sclerosis. Film sequence at 3, 5, 8, and 10 sec. Note retention of barium in mouth with inability to swallow initially. Patchy coating of pharyngoesophageal wall present, with increase in mueus content and salivary secretion. Retention of opaque material in dilated vallecula and pyriform sinuses seen. Narrowing and Fig. 4. Multiple selerosis, Films taken at 3, 4, 10, and 15 sec. Initial retention of bolus and patchy coating of pharyngoesophageal wall seen. Retention of barium in dilated vallecula with dilated pharyngoesophagus seen (4-sec. film). Resegmentation of hypopharynx and cervical esophagus persists through 10-second film, with increase in transit time. sultant prespinal soft-tissue thinning present. Delay in transit time, with generalized residua noted.



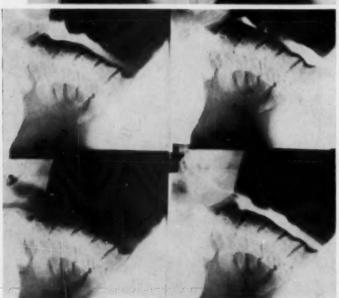
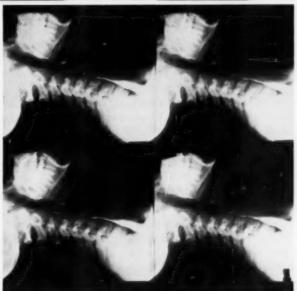


Fig. 5. Myotonia dystrophica. Exposures at 3, 4, 7, and 10 sec. Inability to swallow initially is marked. Pharyngoesophagus is dilated with irregularity of contour. Delay in transit time considerable. Patchy mucus coating present.

Fig. 6. Posterolateral selerosis. Time intervals at 4, 8, 15, and 17 sec. Delay in initiation of swallowing, with dilatation of upper pharynx at inception and delay in transit. Patchy coating with mucus seen. Narrowing pharyngoesophageal junction is apparent. Retention in vallecula noted.

Abnormal Swallowing





tion of pharyngoesophageal area with segmentation noted. Delay in transit time is marked. Small amount of barium Fig. 7. Myasthenia gravis. Films at 4, 8, 13, and 20 sec. Small amount of barium remains in mouth at 20 seconds. Dilataseen in vallecula. Thinning of prespinal soft tissues present.

Fig. 8. Muscular dystrophy. Exposures at 3, 5, 7, and 11 sec. Difficulty in initiating swallowing, with retention orally at Il see. Considerable dilatation of pharyngoesophageal area, with marked retention of barium in vallecula and pyriform recesses. Increase in mucus content apparent.

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junction (most frequently seen in myasthenia gravis and bulbar poliomyelitis).

9. Disturbances in size and shape.

Widening and ballooning

Widening of the epiglottic vallecula with backward displacement of the epiglottis and the ary-epiglottic folds.

Widening of the pyriform sinuses.

Widening of the inferior pharyngeal segment.

Widening of the oropharynx.

Narrowing at the pharyngoesophageal junction

- 10. Insensitivity to boluses either hotter or colder than normal.
- 11. Tendency towards tracheal spillage and aspiration pneumonia.
- 12. Occasional straightening of the cervical spine due to altered posture and position of the head during swallowing, possibly due to spasm of the regional muscles.
- Alteration in prespinal soft-tissue measurements (most often thinning), possibly from pressure of the widened pharynx.
- Occasional forward displacement of the trachea or indentation forward of its posterior wall due to increased lower pharyngeal pressure.

DISCUSSION

No real attempt has as yet been made to correlate specific findings with individual disease. We have not equated the severity of the disease with the degree of roentgen change. In effect, the findings listed above are an all-inclusive summation of nonspecific abnormalities of the swallowing mechanism in neurologic and neuromuscular disorders. Specificity may come later with the accumulation of more material, further experiences, and more advanced technics (cinefluorography, etc.).

Significance of Findings

Although at first glance this work may appear to be only of theoretic interest, such efforts point to practical considerations for the future. This work strongly suggests that patients with central nervous system and neuromuscular disorders frequently show roentgen abnormalities of the swallowing mechanism, which are not always associated with dysphagia. The possibility is suggested that abnormalities in deglutition as herein described may precede clinical detection of the group of diseases studied. Such matters will bear further investigation.

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The roentgenologist may serve an important role in detecting and correlating abnormal oropharyngoesophageal findings in central nervous system and neuromuscular disease states.

Although a seriographic film device such as a Fairchild camera is desirable, with the collection of sufficient data it is conceivable that significant findings in deglutition may be elicited and correctly evaluated utilizing standard fluoroscopic and roentgenographic equipment. More refined technics include cinefluorography and utilization of the new Odelca camera in 70-mm. film strips. One of us (M. H. P.) has had some preliminary experiences with these two new modalities and they appear to offer some promise for the future.

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MEDICAL GRAND ROUNDS

from the VA Research Hospital-Northwestern Medical Center

Psychosomatic Aspects of Peptic Ulcer

E. Clinton Texter, Jr., editor

It is much more important to know what sort of a patient has a disease than what sort of a disease the patient has.—Parry (1755–1822)

Although clinicians and research workers still continue to search for "the cause" of this disease, it must be continuously kept in mind that one of the basic tenets of psychosomatic theory is that the causation of any disease is due to a multiplicity or combination of various factors rather than to one specific, single etiologic agent.—Milton Rosenbaum (1955)

Dr. Craig W. Borden: This morning's conference is to be presented by Doctor Wolf of the Psychiatry Service. Doctor Holt will present the patient.

Dr. Francis J. Holt: The patient, a 32-year-old Negro, was admitted to the hospital complaining of epigastric burning pain of 3 weeks' duration. This pain came on 1–2 hours after meals and was relieved by the ingestion of food, milk, and antacids. He volunteered the information that he worried a good deal, and that his pain is aggravated by emotional difficulties at home.

His past history indicates that his epigastric distress began in 1949. At that time he consulted a private physician and an ulcer was found.

Report of a weekly Medical Grand Round held at the VA Research Hospital-Northsestern University Medical Center, Chicago, III. Presented by staff members of the VA Research Hospital and participated in jointly by the faculty and clinical clerks of Northwestern University Medical School and guests.

Reviewed by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are the result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.

Dr. Craig W. Borden and Dr. Ernest S. Wolf of the VA Research Hospital assisted in editing the conference and Miss Junko Ikeya assisted in the preparation of the conference.

Therapy with the usual bland diet and antispasmodics afforded him relief. He had recurrences in 1953 and 1954 but never had tarry stools or hematemesis.

Physical examination was normal except for moderate tenderness in the midepigastrium, more marked to the right of the midline. A deformed duodenal bulb was demonstrated by the roentgenologist but no crater was found. Basal gastric secretory studies revealed 30 mg. per hour of free acid. This value is within the normal range.

Dr. Wolf, would you like to interview the patient?

Dr. Ernest S. Wolf: First, I propose to give you a little information on the patient's background and then interview the patient. After this we will discuss the patient's particular history more specifically, and later on have a general discussion of the psychosomatic aspects of peptic ulcer.

BACKGROUND OF CASE

The patient is a Negro post-office carrier who was born in the South. His mother died when he was an infant. He does not remember how old he was. When he was 6, his father died. There were five or six children. The oldest sister, who was approximately 10 or 12 years older than the patient, was the one responsible for rearing the family. In his own words the patient said, "I raised myself." He stayed in the South and had most of his education there, and he appears to be a well-educated and rather intelligent young man.

He first experienced symptoms of ulcer when he was in the army, and from then on he had symptoms of heartburn but they were not very severe. He had been working for the post office as a temporary employee before being drafted. When he was discharged, he tried to get his job back but because he had only been a temporary employee he was not rehired automatically. This upset him a great deal, and within the first two weeks after being discharged he had a fairly severe episode of epigastric pain and burning. At that time he reacted in a fairly typical way. He was faced with a situation that he did not know exactly how to handle so he did not look for a job at all and began drinking-"running around," as he calls it. When he was completely broke, he decided to reapply at the post office. He took the Civil Service examination over and was appointed again on a temporary basis. A year later he got a permanent appointment as a post office clerk. During this period of joblessness, and thinking about whether he would or would not get his job at the post office back, he had an acute recurrence of symptoms which later subsided. About a year after this he married. Following marriage, his symptoms again recurred.

At the time that he got married his mother-in-law insisted on a big wedding, which the patient did not want. The wedding cost—I do not recall

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the exact figure—\$2000 or \$3000, and when it was over, the patient found out that his mother-in-law did not have any money but that all the bills for the wedding were coming to him. This he gives as a typical example of his mother-in-law's behavior. He started his marriage in debt, is still in debt, and has been trying very hard to get out of debt.

He describes his mother-in-law as very domineering. One gets the feeling that in describing his mother-in-law he is actually describing his wife; although he does not attack his wife directly as he does his mother-in-law, he frequently says, "Well, my wife is just like her." Since the marriage he has been under a good deal of pressure to live up to the standards of the mother-in-law. He complains that both the mother-in-law and the wife are very impulsive in buying things. He feels that the wife and the mother-in-law pay too much attention to keeping up with the neighbors, trying to be what they actually are not.

In order to handle this situation, where he feels constantly under pressure to please his wife and please his mother-in-law, he took on part-time jobs in addition to his post office job. He worked as a cab driver and as a painter and decorator. Then he opened his own business, a variety store, which he ran part time. Over the last eight or nine years, he has been putting in a work week of fifty, sixty, sometimes more hours, in order to earn what he felt was an adequate income to keep up with the demands that the family made on him. He focuses these demands on his mother-in-law and wife. He has two children, both girls, one aged 7 and one aged 18 months.

I will try in the interview to see whether this pattern of having to be very ambitious, self-sufficient, while at the same time having the need to please and be dependent, can be elicited in the interview situation itself. It was interesting to learn that the nurses on the ward feel that he is very likable. He comes to the nurses' station and brings them gum. He tries awfully hard to please them, and they have the impression that he has the need to give to them in order to be liked by them. This is again part of the same characteristic pattern that he shows in most life situations.

So we will see what the interview will produce [The patient is brought in].

INTERVIEW

DR. WOLF: Have a seat, Mr. Jones. Mr. Jones, this is the medical staff of the hospital. I told you we wanted to talk to you to see how we can best help you. How do you feel about coming down here?

PATIENT: Well, to a certain extent, excitable.

DR. WOLF: Excitable?

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PATIENT: Well, I haven't had occasion to sit and talk before a group of this size before. It is different.

DR. WOLF: Will you tell the doctors a little bit about what brought you to the hospital?

PATIENT: Well, I was having abdominal pains here (indicating stomach) and having sort of distress above my abdomen to a certain extent, sort of burning sensation, with a cramping sensation below.

DR. WOLF: And how long has this been going on?

PATIENT: Well, I would say over a period of seven or eight years . . . I wouldn't detect it seriously all the time. I had probably had some minor symptoms before then, but the pain wasn't too severe.

DR. WOLF: What do you think made it become more severe?

PATIENT: Well, I think that one of the causes was emotional disturbances to a certain extent... something that would happen that would affect me emotionally.... If I was supposed to do something and I found out I could not do it, or it was impossible for me to do it, I would start worrying about the reason that I couldn't do it.

DR. WOLF: You were supposed to do something?

PATIENT: Yes, when I say "do something," I mean if there was a responsibility or something that I was supposed to effect in some instances and I couldn't meet it. . . . If I had a bill to pay and I couldn't pay it, I would worry about it. If there was some circumstance that prevented me from paying it, I would get upset as to why I couldn't do it. I would figure out why I couldn't. I knew why I couldn't.

DR. WOLF: You knew why you couldn't?

PATIENT: Well, I didn't have the money, and there were other circumstances that prevented me from having the money. . . . I had too many other obligations. I had so many that perhaps I couldn't wholly fulfill them all as I would have liked . . . financial obligations and domestic obligations—just things that face the ordinary person, I imagine. But I wasn't capable of accepting them. There are a lot of people I imagine that do not let things affect them in that respect. But I figured that if you are obligated, you are obligated.

DR. WOLF: You mentioned domestic obligations?

PATIENT: Well, every married man I imagine has certain domestic obligations and must fulfill them the best he can. If he finds or thinks that he isn't fulfilling them to the best of his ability, I imagine he gets disturbed one way or another.

DR. WOLF: Did you feel you were not fulfilling your obligations to the best of your ability?

PATIENT: Well, I would say I did, because I couldn't do any better.

DR. WOLF: What sort of work have you been doing?
PATIENT: I have been working for the post office.

DR. WOLF: How are things going at work?

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PATIENT: Fine.

DR. WOLF: Will you tell us a little about your other jobs?

PATIENT: Well, over a period of seven or eight years, I would say, up until about a year ago, I had been working in addition to my regular job, on some other jobs. I was a drug apprentice for a length of time, and I have driven a cab part-time, and over a year ago probably, I did a little decorating.

DR. WOLF: That is working pretty hard, isn't it?

PATIENT: Well, I imagine it is. I probably did not realize it... Well, I realized it, too, because I figured that doing all of this work was associated to a certain extent with my symptoms... Well, I know I wasn't eating right, and perhaps I wasn't resting right.

DR. WOLF: Why weren't you eating right?

PATIENT: When I was working at the drug store I would get off from my regular job at five o'clock, or five-fifteen, and I would be at the drug store at six o'clock. I didn't have time to go home and eat, so I would grab a bite to eat on the way.

DR. WOLF: What time would you leave for work and get home from work?
PATIENT: I would leave home at approximately eight o'clock and get home at approximately ten-thirty, or a quarter to eleven.

DR. WOLF: How did your family feel about that?

PATIENT: Well, it was mentioned to me by my wife several times, but I imagine she knew that the reason I was trying to do this, and she more or less went along with me. . . . She didn't directly tell me to stop, she didn't persuade me to stop, but maybe sometimes she would say, "Don't you think you are overdoing it?" or something like that, or "You're overdoing it a little. You will work yourself to death."

DR. WOLF: What made you work so hard, if it wasn't your wife?

PATIENT: Well, the only thing I can say is the ability to acquire the amount of income, because I seem to have always been short. I was thinking that perhaps if I had another job or something I could go along more smoothly. DR. WOLF: What is your wife like?

PATIENT: Well, she is not bad. I mean she is easygoing. She is good to me I think although she might not show it as I would expect it....[by that] I mean there are sometimes some things that you would expect of a wife, some way that you would expect her to respond to certain things, and when they don't you are just disappointed, that is all.

DR. WOLF: What do you mean, you get disappointed?

PATIENT: Well, on one occasion I would probably give her money to pay a bill and she said she paid the bill and she probably didn't. She says she will do it and she doesn't.

DR. WOLF: When did the symptoms start this time?

PATIENT: I would say a week or ten days before I was admitted into the hospital.

DR. WOLF: How have you been feeling since you have been here?

Patient: Fine, with the exception of once I seemed to get the same symp-

toms . . . when I was out on a pass and I didn't eat as frequently when I was out as I did here.

DR. WOLF: Where were you born?

PATIENT: I was born in Ellington, Georgia.

DR. WOLF: Tell us a little about your family.

PATIENT: Well, my parents died when I was small. My mother, I don't remem-

ber. My father died when I was approximately six or seven.

DR. WOLF: You do not remember your mother at all?

PATIENT: No, I cannot remember her at all.

DR. WOLF: What is the earliest thing you can remember?

PATIENT: Well, I remember as a kid attending church frequently.... And I remember that at one time as a small child I was told by my father not to go because I was sick, and I went anyway... well, he said I was sick. I wasn't old enough to know whether I was sick or not.

DR. WOLF: You didn't feel sick?

PATIENT: I don't know whether I did or not. I couldn't say. But I just remember the incident because it stood out in my mind.

DR. WOLF: And how are you feeling today?

PATIENT: I feel fine.

DR. WOLF: How long do you suppose you will be in the hospital?

PATIENT: Well, I understand that perhaps the early part of next week, I will leave.

DR. WOLF: And what are your plans?

PATIENT: To go back to work.

DR. WOLF: Thank you very much for coming down and talking to us [The patient left].

Dr. Wolf: The interview today fairly well highlights the main problem that we can focus on.

Comment

I thought it was very interesting that his pressure to go to work was a pressure that came from within, from the patient himself, even though he was doing this in order to satisfy financial or domestic obligations. He apparently was not too willing to go into the details of what he meant by domestic obligations. However, the pressure was not from the family direct, but the pressure came from pride or a necessity to please the family.

While he was doing this, the job kept him away from home a good deal of the time, which implies that he did not receive the kind of gratification that one usually gets from family life. It is interesting that his symptoms subsided rather rapidly after admission to the hospital and recurred within a few hours after he went home on pass. In the hospital he feels secure and taken care of, with quick relief from

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symptoms, but as soon as he returns home he is again confronted with the feeling of needing to take care of others rather than being cared for himself. The result is almost immediate recurrence of symptoms. We see this pattern in many patients with different diseases where the problem of dependency is a prominent psychologic feature in the personality structure.

When I asked him about his wife, he started out by saying "She's not bad." This is a negative statement. She had not been accused of being bad, but he immediately defended her against any accusations, which leads me to speculate that actually he is not as enamored of his wife as he might consciously say. In his mind he had apparently accused her of those things against which he spontaneously defended her.

When you then look longitudinally at the history of his symptoms, the first severe exacerbation occurred when he was discharged from the army. The army presents a secure sort of environment for many people. Being on his own all of a sudden and not having the job to come back to that he had expected, he had a flare-up of symptoms. When the job situation settled down, his symptoms settled down. His symptoms again increased over the last seven or eight years during the period that he has been married. During these years the need of wanting to be secure and dependent has conflicted with his need to be independent, ambitious, and to provide well.

If we seek the origin of this, we can speculate as to what happened when he was an infant. His mother died when he was an infant. One wonders whether the person or persons who did take care of him really gave him the kind of satisfaction that a baby needs, the kind of feeling of security that is essential for emotional growth. Then when he was 6 years old he lost his father. The sister who reared him was not enough older than he that she could have been very motherly. He did not receive the kind of upbringing that children need in order to mature emotionally.

In summary, this man presents himself overtly as ambitious, independent, and conscientious in taking care of his family, while at the same time we note that his symptoms flared up when his life situation made him feel insecure, when he had the subconscious need to be taken care of, a need which both his circumstances and his pride in being selfsufficient would not allow him to indulge.

I should now like to discuss the general psychosomatic aspects of peptic ulcer.

PSYCHOSOMATIC ASPECTS OF GASTRIC FUNCTION

Historical Notes

William Beaumont¹ in 1833 recognized that changes in gastric functions were associated with altered emotional reactions, but he was concerned chiefly with observations of gastric juices. Stiller in 1884 first pointed out the frequency of psychogenetic factors in gastric disturbances, stating, among other things: "That people develop gastric disturbances after financial losses and suffer from them until their financial conditions turn to the better are every day experiences."

W. B. Cannon, the great physiologist, wrote in 1909 in a paper on the influence of emotional status on the functions of the alimentary canal: "The sudden changes wrought by these emotional disturbances are not brought to consciousness, and are clearly known solely through physiological studies." In this he clearly foreshadowed the modern concepts of the psychology of peptic ulcer.

Psychologic Mechanisms of Dysfunction

The most important contribution in this area stems from psychoanalytic study. The first contact the infant makes with the outside world which becomes meaningful emotionally is established through the feeding process. The infant experiences his first relief from physical discomfort and tension through nursing, and the satisfaction of hunger through this experience becomes deeply associated with feelings of well-being, security, and being loved. Thus, for the infant, being fed is equated with being loved, and the physiologic pathways associated with the feeding process become intimately associated with the total emotional state of well-being. Frustration of these oral-receptive impulses usually creates tension and mobilizes oral-aggressive impulses, which are manifested by biting, taking, greed, and envy. Aggressive impulses are characteristic of the weaning process, and with the development of teeth, hostility in the form of oral aggression becomes quite apparent. These oral-receptive and oral-aggressive emotions may become inhibited and repressed due to intrinsic (shame, guilt, fear, pride) and extrinsic (fear of persecution, loss of love) factors. When these drives are blocked they must find another outlet and may, in the attempt, focus on the psychologic pathway with which they were originally associated, creating a state of permanent tension. In this way inhibitions and stimulation of psychological pathways of the upper gastrointestinal tract on a psychologic basis may give rise to various types of gastrointestinal disturbances.

Psychosomatic Correlations

Heyer² reported observations in patients with gastric fistula and observed effects of pleasant and unpleasant psychic stimuli on gastric secretion. He hypnotized his subjects and inserted the gastric tube under deep hypnosis. Suggestions were then given about eating various foods and secretions collected. In the course of these experiments, the subject experienced vivid affects which regularly disturbed the gastric flow irrespective of their euphoric or dysphoric nature. Similar experiments by Heilig and Hoff,⁴ also using hypnosis, demonstrated that the nature of gastric secretion is not in all cases specific for the food but is dependent, to at least the same degree, on the attitude of the individual.

Wolf and Wolff⁶ demonstrated that emotions involving hostility, resentment, and anxiety were accompanied by increased secretion, motility, and vascularity, while emotional states of fear, sadness, and other affects associated with desire for withdrawal were marked by depression of these gastric functions. The emotional reactions observed were conscious and for the most part, the experimental subject was fully aware of them. Although tension arising from conscious or expressed emotional states plays an important role in psychosomatic problems, it is the tension arising from repressed and unrelieved psychologic drives which plays the more basic role in these disorders.

Mirsky⁶ has attempted to correlate psychosomatic factors with the function of the gastric mucosa by measuring pepsinogen in the urine and blood. Daily urine specimens were taken from subjects for as long as two years. Six subjects were in analysis, 3 in psychotherapy, and 18 were "normal" men who were interviewed at intervals and kept a diary of daily events and of the emotional reactions to various life situations. Mirsky inferred that dependency longings in a life situation which threatens the dependency needs of an individual mobilize unconscious urges and are associated with increased gastric activity. He was unable to correlate the secretion of pepsinogen by the stomach with the awareness of chronic emotional reactions of a varied sort, but interpreted it rather as a response to life situations which stimulated strong unconscious oral-receptive and dependent longings. Margolin in similar studies, confirmed Mirsky's correlations.

The Specificity Problem

Alexander^{8, 9} has proposed that ulcer patients have a specific type of emotional conflict. He postulated that being fed becomes equated with being dependent in the infant, and therefore if in a later period of life an intense need to be dependent on others is frustrated, it might be

expressed in the wish to be fed. Under such persistent stimulation, the stomach behaves as if it is constantly prepared for food, with the result of hypersecretion and hypermotility. There is frustration of the need to be dependent on others, either internally by shame, pride, or guilt, (where the patients have over-compensated by being aggressive, ambitious and independent) or externally by the patient's environment.

Rosenbaum and co-workers10 studied 20 unselected men with peptic ulcers. Parasitic dependent desires were found in every patient and the origin of such strong dependent wishes was traced to either rejection or spoiling in early childhood. The ulcer symptoms developed when these infantile cravings were denied. On the basis of overt personality structure, the patients were divided into three groups. The first group reacted to deep unconscious dependent cravings by becoming ambitious and successful (the classical "ulcer personality"). The second group of patients reacted to similar dependent desires by giving in to them partially. As a result they appeared passive and shy, with marked trends toward feminine identifications. The third group expressed their strong oral cravings and demands by "acting out" as well as by their symptoms. They indulged in drinking, gambling, delinquency and were unable to earn a living. They had a little or no guilt about selfish or demanding impulses. This is the unweaned suckling type of personality whose oral needs may be insatiable. Although the conflict situation was similar in all these patients, the resulting personality façade varied from independent attitudes to parasitic dependence.

Mahl¹¹ has challenged the concept of specificity as formulated by Alexander and his group and has suggested that the most important factor in the pathogenesis of peptic ulcer is chronic anxiety or fear.

Therapeutic Implications

The physician who practices comprehensive medicine is aware of the importance of emotional factors. In an effective physician-patient relationship, the physician should understand the crucial current areas of conflict so that he will be in a position to meet the emotional needs of the patient. The repressed dependency needs of many patients, especially those with gastrointestinal complaints, can be gratified either directly or indirectly without necessarily inducing shame or guilt in the patient. This can be done by environmental manipulation, by a secure physician-patient relationship, and by giving medication. Selected cases can be referred to psychiatrists for more intensive psychotherapy. It is important to remember that chronic unsatisfied dependent needs may have to be gratified by the physician for a lifetime.

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GENERAL DISCUSSION

Dr. Borden: Very good. Thank you, Dr. Wolf. Would you care to comment, Dr. Texter?

Dr. E. Clinton Texter, Jr.: There are a number of questions that we would like to have answered. Ulcer and hypertension frequently coexist, and it has been postulated that similar mechanisms operate in these two conditions. What is the relationship of the psychodynamics of peptic ulcer to the psychodynamics of hypertension? Both have been termed "stress" disease. What determines a target organ? Why does one patient develop an ulcer, another hypertension, and a third develop both when the psychodynamics are very much the same? Is there any difference in the personality of these people prior to developing an ulcer and after developing an ulcer? Most studies have been done on people after the ulcer has developed. We need more objective studies on the mechanism of pathways.

Dr. Wolf: I would like to comment a little bit on this matter of predisposition, or whatever it is. This is certainly a problem that has not been solved, but some work by Dr. Mirsky may lead eventually to a clarification. In doing pepsinogen studies on large groups of people, he found that the levels of pepsinogen would group themselves around two levels. All the ulcer patients were within the high-level group. As they followed these patients along longitudinally, they found increased pepsinogen levels associated with the life situation that stirred up subconscious dependent needs. When the specific psychologic conflict in this group of people is added to a constitutional predisposition of an increased pepsinogen level, an ulcer may develop. The others do not have the increased pepsinogen level to start with. Maybe these will develop hypertension. They are now testing cord bloods from newborn infants and following these infants along. The pediatricians are aware that ulcer is not just a disease of adulthood but also of children.

Eventually I am sure we will find in other psychosomatic illness that some difference probably determines whether the end result will be ulcer, or hypertension, or some other organic disturbance.

Dr. Texter: I do not have an ulcer myself, but it is probable that there are people here who do have an ulcer, and I imagine many people would find this concept of ulcer an unpalatable one. Would you like to elaborate on that?

Dr. Wolf: I do not see why it need be unpalatable. I have heartburn occasionally. My father had an ulcer. Eventually maybe I will have one. I do not think that particularly bothers me. We all ought to be mature enough to accept that we have dependent needs.

Dr. Texter: You said the ulcer patient was unable to accept the fact that he had dependent needs.

Dr. Wolf: Well, in many ulcer patients that is true. They are disturbed by this because they cannot accept their own dependent needs. What is there so bad about wanting to be a baby occasionally? One should not think that a specific conflict, the one that we have pointed out, is the whole answer to this problem. We can only think of it as one among many factors which combine to produce the final disease picture.

Dr. Hugo C. Moeller: Is there any difference in the psychodynamics of peptic ulcer of the stomach or the duodenum?

Dr. Wolf: I do not know.

Dr. Moeller: In Rosenbaum's classification, the classical type, the ambitious, the self-reliant type is described. Is there any information in regard to recurrence in those individuals, in distinction to the other two groups?

Dr. Wolf: I have not seen any statistics on that, either.

Dr. Moeller: It would seem that the self-reliant types would be reluctant to follow a medical regimen and therefore might be more likely to return with bleeding or perforation.

Dr. Wolf: I would imagine, speculating from the personality structure, that the classic ulcer type *would* have more difficulty, because he is independent. He is not going to follow the medical regimen, and he is not going to go after the gratification he needs. The patient who is willing to accept his dependent needs is more likely to get them satisfied. He is more likely to stick with the doctor, more likely to come to the hospital, and therefore more likely to get good attention and good care than the other patient.

Dr. W. James Kuhl: Suppose we were to reverse the coin. How many patients with dependent needs that are unsatisfied will develop peptic ulcers?

Dr. Wolf: I can't answer that, either. Dependent needs certainly are not the only factor involved. They are found in many patients with other diseases. But I have yet to see an ulcer patient where these problems were not prominent, and one has the impression that they are one of several necessary factors that result in the disease picture.

Dr. David P. Earle: That is a fairly important question, isn't it [the problems of controls]? I think that we will all agree that psychodynamics play a large role in diseases such as peptic ulcer, but I still would like to see the very question that Dr. Kuhl has asked answered.

Dr. Roy M. Whitman: The main hypothesis that has to be really presented and stressed is that of multiple-factor diseases. One person

with a very minor dependency conflict may have such a high level of acid secretion that the conflict is a very unimportant factor. In another with a fairly low secretion the conflict is the significant thing. So you can see all the varying proportion that might combine to make for an ulcer, and of course, it makes the problem very difficult.

Dr. Leonard A. Kratz: Between 1932 and 1953, when I was in active surgical practice, I encountered 1 stillborn baby with a perforated duodenal ulcer and 9 cases of pneumoperitoneum secondary to peptic ulcer in the newborn. I do not believe any of them were psychogenic. **Dr. Texter:** Psychiatrists tell us psychogenic factors may operate in utero.

Dr. Morris A. Lipton: I think what Dr. Whitman has reiterated is that everyone would like to have one single causality. This would make life so simple. You get a streptococcus infection, then you develop rheumatic fever. Unfortunately, with some diseases it is not quite so simple. There may be a multicausality.

What is a child going to be like if he is born with a high pepsinogen, who has perfectly normal parents who try to gratify him? He may not be gratified no matter what they do for him. This can lead to personality disturbances from the day he is born. Some people who look as though they never received adequate gratification really received plenty. It may not have been enough for their purpose because they happened to be that way genetically.

When you are treating patients with peptic ulcers you are not treating a statistical problem, you are treating an individual patient. You have to evaluate in the particular patient the extent to which his ulcer may be genetically determined, environmentally determined, or what have you. All of these parameters are valid parameters in the case of the ulcer.

Dr. Earle: Can I make one comment on that? You say it is very nice to think that rheumatic fever is due to a streptococcus infection but there are many other factors. You will admit rheumatic fever is due to streptococcus. There are other factors that determine how sick you are, but the disease is due to the streptococcus.

I presume that Dr. Wolf used the quotation by Parry as referring mainly to psychosomatic fields. If somebody breaks his leg, it is really much more important to know how to fix the leg than what kind of a person he is in that particular problem.

Dr. Borden: That is true. But it is also true, Dr. Earle, that if you visit a fracture service in this type of hospital, you will find most of the

patients have a specificity in personality type. There is usually a good reason why the individual broke his leg.

SUMMARY

- 1. The psychosomatic approach to medical problems is as old as medical practice.
- In recent years a revived interest in mind-body relationships has led to a scientific formulation of the psychologic factors in medical illness.
- A rudimentary understanding of the psychology of the functions of eating and eliminating is essential to an understanding of psychosomatic factors in gastrointestinal diseases.
- 4. Our present-day understanding of the psychology of eating and excretory functioning, though incomplete, is derived from psychoanalytic investigations.
- 5. Clinical and experimental investigations have demonstrated correlations between emotions, and gastric secretions and motility.
- 6. A specific psychologic conflict has been reported to be associated with peptic ulcer in patients studied by psychoanalytic type of investigation.
- 7. The theory derived from these studies proposes that physiologic sequences resulting in peptic ulcer are activated by subconscious dependent needs; these needs are frustrated either by internal factors, such as pride, shame, and guilt, or by external environmental factors. The specific conflict is between the subconscious dependent needs and the factors that frustrate its gratification. Critical evaluation of this theory has produced much clinical evidence in its favor; however, the lack of adequate controls and the recognition of other factors have obscured the picture.
- Research now in progress may clarify the problem of "specificity."
- 9. The concept of multiple factors in causation of disease seems to be crystallizing as more evidence is obtained. Treatment of peptic ulcer, in order to be rational, should be based on an understanding of the psychologic factors as well as the other factors involved. A good doctor-patient relationship satisfies many unconscious needs and is a most important tool in the treatment.

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EDITORIAL

Personality and Peptic Ulcer

FOR A GOOD MANY YEARS there have been references in the medical literature of an ulcer type of personality, but the outlines of this type have never been brought clearly into focus so that the patient with ulcer could be sharply distinguished from other types. Ulcer patients nevertheless do seem to share certain characteristics of appearance, behavior, and attitude which have become widely accepted as typical. Shakespeare described the lean and hungry look of Cassius in Julius Caesar and, although nothing was said about an ulcer, Cassius has been taken as the prototype of the ulcer personality. Caesar, who was made somewhat uneasy by Cassius, said, "Let me have men about me that are fat; sleek-headed men and such as sleep o'nights. You Cassius has a lean and hungry look; he thinks too much, such men are dangerous." It is likely that Caesar saw Cassius as an ambitious and aggressive person, and that Cassius saw Caesar as one who aroused his competitive instincts. More patients with peptic ulcer have a lean and hungry look than not, and there is something highly competitive about most of them. However, since vast efforts to delineate a personality "profile" for peptic ulcer by psychologic testing procedures have failed, many investigators have been led to conclude that there are no common denominators of personality among those with peptic ulcer. This inference is not altogether justified, since we have not arrived at a generally accepted concept of what a "personality type" is. Moreover, there is no firm evidence that present-day psychologic testing procedures are capable of making such a distinction.

Perhaps light can be shed on the attitudes and way of life of the ulcer patient by considering what is going on in his stomach. The condition of the stomach of the ulcer patient is continually that which prevails only for short periods in a normal individual who is about to be fed or about to devour. The stomach of the healthy person resembles that of the ulcer patient only when it is hungry. When the hunger of the healthy individual is satisfied by food the overactivity of his stomach subsides. The stomach of the ulcer patient, however, is in a state of increased gastric function more or less continuously, regardless of meals. The

pangs of hunger are relieved as long as food remains within the stomach but quickly recur when the stomach is empty again. Thus the stomach of the ulcer patient is in an exaggerated and sustained state resembling hunger.

The psychoanalysts have felt that the competitive aspect of the patient with peptic ulcer is a personality development which hides an underlying feeling of dependence and longing for support. Oddly, the overactive stomach can be viewed in either way—as a symbol of a biologic need for sustenance or as reflecting a wish to devour. Perhaps both are pertinent to the bodily pattern which ends in ulcer.

Numerous attempts have been made to explain why some individuals in a setting of significant emotional conflict develop troublesome gastric overfunction and, perhaps, peptic ulcer, while others may develop precisely the opposite changes in the stomach marked by decreased acid production and slow emptying with nausea, and still others develop other physiologic disturbances but no evidence of gastric disorder. Analysis of the conflict situation has not been fruitful, and neither have attempts to construct a constitutional or personality profile been successful in delineating very sharply between those who develop and those who do not develop peptic ulcer. It has been more profitable to examine and characterize the way in which the individual habitually met threats and challenges in his life situation. Nevertheless, it cannot be said that the "cause" of peptic ulcer has been identified. The "cause" may be the algebraic sum of a number of factors including, perhaps, hereditary predisposition, psychologic vulnerabilities because of defective early emotional development, important conditioning experiences, and so forth. The ulcer may follow a specific stressful event but the reason for the occurrence of gastric overfunction instead of some other reaction pattern may be hidden in the nature of the man himself and therefore in the peculiar significance of the event to him. A blow on the cheek from the glove of an adversary is a straightforward enough stimulus, and yet from it one could not predict what the reaction would be of the one who was struck. The reaction would not depend exclusively on either constitution, temperament, or experience. Many factors would enter in to determine which of several possible courses of action open to him he would elect. He might choose pistols, sabres, or boxing gloves, or he might run away, or even collapse at the feet of his challenger, or sidestep the incident by retracting or making a joke of it. Why he chooses one course rather than another depends upon a myriad of factors including his inherited tendencies, his early experiences, his cultural background, his habits and skills, and so on. Similar considerations taken together probably determine whether or not and to what extent a man will react to troublesome life situations with an acceleration in the functions of the stomach. The significant point is that such reactions do occur often enough and that they have significant implications for health and survival.

It is important to bear in mind that transient stresses which produce anger and resentment, while capable of inducing short-lived overfunctioning of the stomach, are probably not the ones concerned with the development of ulcer. Much more chronic stresses of which the patient may be unaware but which produce sustained gastric overfunctioning 24 hours a day are much more likely to be the factors which operate in the combination of forces which brings about peptic ulcer. Again, this does not mean every chronic stress. Some stressful circumstances appear to provoke underfunctioning of the stomach. For example, those who had an opportunity to study illnesses among prisoners of war exposed to starvation and torture at the hands of the Japanese and Germans during World War II found an actual reduction in cases of peptic ulcer. However, in uncaptured Britain during the height of the bombing the incidence of peptic ulcer rose sharply. Groen, working among the Dutch in concentration camps during the German occupation, was able to study persons who had been patients of his before the war. Those with peptic ulcer actually improved in the anguished, but nonetheless inflexible and predictable circumstances of the prison camp, only to flare up again when the war was over and they were thrown back into their former social setting with its peculiar challenges and insecurities. Groen's work and the work of others also point up the comparatively minor importance of poor food in provoking ulcer symptoms, since the prisoners ate the roughest kind of food and very little of it, while Dutch civilians in peacetime place great emphasis on eating good food and especially dairy products.

Finally, it would not be possible to appraise the role of personality in peptic ulcer without taking into consideration the "unconscious." It is about as difficult to visualize the unconscious as it is "the little man who wasn't there." One famous psychiatrist defined the unconscious as "the place, that isn't a place, where a thought is harbored before it becomes a thought." Seriously, however, despite semantic problems, there can be little doubt that important mental activity goes on within the human brain altogether without awareness. The processes can be conveniently thought of in terms of (1) "receptor ac-

tivity"—that is, receiving impulses from our surroundings and registering them in the brain: (2) "integrative activity"—that is, the connecting up of receptor impulses with circuits previously established by experience or acquired attitudes; and (3) "reaction formation"—that is, the bringing into play of some sort of bodily response, a tear in the eye, a sigh, or a sudden stopping of activity in the stomach with its characteristic "sinking feeling." A variety of thoughts and emotions may occur as part of "reaction formation" without being connected in awareness with the stimuli that set them off. Unconscious receptor activity is commonly experienced, as when a scientist looks down the barrel of a single ocular microscope with both his eyes open. The light rays are registering two images on his brain, one from the microscope and the other from the table along side it, but the person is aware only of the former. Practice has blotted out the extraneous image from consciousness. Unconscious "integrative activity" and "reaction formation" can be recognized in the occasional effects of a certain melody on a person. The associations of the melody may be long forgotten (unconscious) but they still exist as circuits in the brain enabling its nostalgic power to produce a variety of reactions in the individual without any awareness of how or why they came about.

Those experiences which are concerned with emotional and character development in infancy and early childhood and the associations and reactions that went with them are largely unconscious in most of us but nevertheless appear to help shape our thoughts and behavior throughout our lives. They often determine whether or not an experience in adult life is stressful.

Many important and relevant life stresses may not be immediately manifest in a patient with peptic ulcer despite his desire to be altogether frank and introspective. The brain in all of us is able over the years to bury in the unconsciousness our most troublesome conflicts and problems so that by lack of awareness we are at least partly protected from them. They still exist, however, as potentially powerful circuits in the brain, capable of being touched off and setting up a variety of responses, among them overfunctioning of the stomach and perhaps peptic ulcer.

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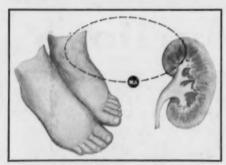
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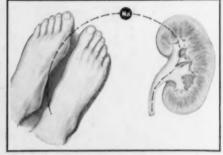
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